



The genus *Mussaenda*: A phytopharmacological review

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ABSTRACT

The use of medicinal plants has gained more importance because of its natural origin and high therapeutic significance. The various species of the genus *Mussaenda* has many novel phytochemical constituents which has high pharmacological activities such as anti-inflammatory, antioxidant, antimicrobial etc. useful for the treatment of many health disorders. This review describes the importance of the genus *Mussaenda* and various experimental research carried out in different species of this genus which will provide information to develop a new herbal drugs.

Keywords: Medicinal plants, Phytoconstituents, Pharmacological activity

INTRODUCTION

Traditional medicine has been used for a long time of history which serves peoples all over the world. The ethno botany provides a rich resource for natural products which provides a step stone for drug research and development. In recent years, the use of traditional medicine of plant source has gained more interest. It has been reported that more than 50% of all modern drugs in clinical usage are of natural products. The medicinal plants have been comprised about 8000 species and among them 50% accounts for higher flowering plant species of India which is yet to be explored [1]. These plants have been used for the treatment of various diseases for many years. Terrestrial plants have been used as medicines in Egypt, China, India, Greece and it has been proved to be an excellent reservoir of new medicinal compounds [2]. The medicinal activities of many herbal plants have been well documented in ancient Indian literature[3] as Ayurveda, Siddha, Unani systems of medicine which provides a good base for scientific exploration of new drugs [1]. In this regard, the pharmacological activity of different species belongs to the genus *Mussaenda* were briefly discussed which will provide a knowledge to develop a new drug based on natural products.

2. Importance of the genus *Mussaenda*

The genus *Mussaenda* is an important source of pharmacologically active natural products, particularly iridoids, triterpenes and flavonoids. The advantage of the species of this genus is easier growth, pest and disease free and can withstand heavy pruning. Their medicinal activities includes cytotoxicity, anti-inflammatory, antiviral, antioxidant and antibacterial properties [4], diuretic, antipyretic and effective in laryngopharyngitis, acute gastroenteritis and dysentery and also anti-fertility activity [5].

3. Distribution of the genus *Mussaenda*

The genus *Mussaenda* is native to West Africa through the Indian sub-continent, South East Asia and Southern China. The distribution of some important species such as *M. frondosa*, *M. incana* were widely distributed in Central Nepal, India and Srilanka, *M. macrophylla* and *M. roxburghii* were found widely in Central and Eastern Nepal, *M. raiatensis*, a native species of Tonga occurs in open places on ridges, in coastal to lowland forests, *M. pubescens* were found in shady hillside, valley and shrub jungle of East, South and Southwest China [4]. *M. hossei*, *M. Multinervis*, *M. erosa*, *M. laxiflora* were native to china [6, 7].

4. Taxonomical classification

The taxonomical classifications of the genus *Mussaenda* were as follows:

Kingdom: Plantae
Division: Angiosperms
Class: Eudicots
Subclass: Asterids
Order: Gentianales
Family: Rubiaceae
Genus: *Mussaenda*

5. Pharmacological and phytochemistry of *Mussaenda* species

The pharmacological activities and phyto constituents of different species of the genus *Mussaenda* were briefly discussed and as follows:

5.1. *Mussaenda philippica*:

The phytoconstituents isolated from the sepals of *M. philippica* were identified as three iridoid glycosides such as 5-hydroxy davisiosides, 4-acetoxy-7-methoxy secologanin and 6-methoxy mussaenoside as well as two flavones, 5,7,4'-trihydroxy-3'-methoxy flavone and 5,7-dihydroxy-6, 3',4'-trimethoxy flavone [8].

The different parts of this plant is useful for various treatments such as bark is used as remedy for stomach ache, dysentery, leaves for lung and chest infections, full-grown sepals for jaundice [9].

The methanolic extracts of leaves of *M. philippica* along with ten medicinal plants of Bangladesh were screened for evaluating analgesic activity in mice. The peripheral analgesic activity of the samples were evaluated in mice using acetic acid induced writhing method and the result shows the plant extracts were able to reduce the writhing significantly ($P < 0.05$) at a dose of 400 mg/kg body weight after oral administration. The methanol extracts of *M. philippica* inhibited acetic acid-induced writhing effectively with percent inhibition of 76.1 [10].

Melfei Estrada Bungihan and *Claribel Asuncion Matias* studied Antioxidant, Phytochemical and antibacterial activity of *M. philippica* Flowers. The ethanolic crude extracts were subjected to phytochemical screening, determination of total phenolics expressed as mg AAE/g sample by Folin-Ciocalteu method and Radical scavenging activities were measured using DPPH assay. The results showed the presence of 3 phenolics, 1 alkaloid and 3 terpenoids, total phenolic content of flower showed 57.50 mg AAE/g sample, Radical scavenging activity of the flower extract is 75.0 % with the IC_{50} value of 344 ppm. The flower extract also shows antibacterial activity against *Staphylococcus aureus* [9].

The methanolic extract of leaves, stem and bark shows activity against *Bacillus subtilis* [11] and the ethyl acetate extract of *M. philippica* sepals (400 mg/kg) has anti tumour activity against Caco-2 cell line in male mice for colon cancer and MCF-7 cell line in female mice for breast cancer [12].

5.2. *Mussaenda arcuata*

The phytoconstituents in the methanolic extract of *Mussaenda arcuata* leaves were identified as four flavonoid glycosides astragalgin, isoquercitrin, kaempferol-3-O- β -D-rutinoside, rutin and two phenylpropanoid derivatives melilotoside and dihydromelilotoside [13].

The whole plant is useful for the treatment of febrifuge, depurant, asthma, purgative, albuminuria, dermatosis, conjunctivitis, gastroenteritis [14] and leaves for fever and inflammation [15]. The chewing of *M. arcuata* increases salivary flow, an action known to benefit both hard and soft tissues of the mouth [16]. The decoction of the root is used for the treatment of pre hepatic jaundice when it is administered orally and if it is applied externally, it is used for the treatment of skin rashes in babies [17].

The antioxidant and free radical scavenging activity of *M. arcuata* were evaluated using the methanolic and dichloromethane extracts of leaves and stem. The result shows methanol and dichloromethane extracts of leaves has moderate activity for both DPPH radical scavenging assay and antioxidant assay (β carotene assay) and the extracts of stem has weak activity for both assays [14].

5.3. *Mussaenda erythrophylla*:

The phytoconstituents identified from the ethyl acetate extract of the stems of *M. erythrophylla* were β -sitosterol, 5 hydroxy-7, 4'-dimethoxy flavones, 3- iso cumaryloxy -cyclopropane-1-oic acid and 4 -hydroxy-3-methoxy cinnamic acid [18]. The roots of this plant is useful for cough, jaundice and when chewed acts as an appetizer [5].

The anti-arthritic activity of *M. erythrophylla* plant extracts was evaluated by proteinase inhibition and denaturation assay and it was found to be effective to protect *in vitro* arthritis [19].

The ethyl acetate and methanol extracts of *M. erythrophylla* was tested for *in vitro* anthelmintic activity on the earthworms (*Pheretima posthuma*). It significantly exhibited paralysis in doses (10, 20, 40 & 80mg/ml) and also caused death of worms especially at higher concentration of 80mg/ml as compared to standard drug (piperazine hydrate) [20].

The diuretic effect in chloroform and ethanolic extracts of *M. Erythrophylla* root in normal rat was investigated. The extracts of roots were administered to experimental rats orally at doses of 250 and 500 mg/kg and Furosemide (10 mg/kg) was used as positive control in their study. It was observed that urine volume was significantly increased and the result concludes *M.erythrophylla* can be used as a diuretic agent [5].

The ethyl acetate and methanolic extracts of *M.erythrophylla* possess hepatoprotective activity against CCl₄ induced hepatotoxicity in rat. This was evident from significant reduction in serum enzyme, SGOT, SGPT, ALP and Total bilirubin (TB) [21].

5.4. *Mussaenda pubescens*

The phytoconstituents isolated from the aerial parts of *M. pubescens* were identified as two novel triterpenoid saponins, mussaendosides U, mussaendosides V [22] and two new cycloartane-type triterpenoidal saponins, named mussaendosides M and mussaendosides N [23]. Rotundic acid, a family of triterpenoid was also isolated from *M. pubescens* which is found to have cytotoxic activity [24].

M.pubescens has antiviral activity against respiratory syncytial virus [25] and also has antifungal activity against *Phytium ultimum*, *Rhizoctonia solani*, *Aspergillus fumigatus* [26]. *M. pubescens* has been used as a diuretic, antiphlogistic, diaphoretic and antipyretic agent, and it has also been used to detoxify mushroom poisons and to terminate early pregnancy. The most abundant saponin mussaendoside O from *M. pubescens*, can inhibit the secretions of the lachrymal and salivary glands induced by galanthamine, and it can also inhibit the contraction of the isolated longitudinal muscle strip from guinea pig ileum evoked by an M-Ach receptor agonist (carbachol, 10⁻⁶ M) at concentrations of 10⁻⁴ and 10⁻⁵ M. Therefore it acts as an antagonist of the M-Ach receptor and also it has immunopromotive and hemolytic activities [27].

5.5. *Mussaenda frondosa*

The phytoconstituents identified by GC MS analysis of ethanolic extract of *M.frondosa* has twenty chemical constituents. The major chemical constituents were identified as (-)-Quinic acid (32.87 %), 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol (8.30%), Naphthalene, decahydro-2-methoxy-(7.20 %). 1, 2, 3-Benzenetriol (7.70%). It has various pharmacological activities such as antiseptic, antioxidant, antidermatitic, fungicide, insecticide, anti-tumor etc.[28].

The leaves are effective for the treatment of jaundice, asthma, hyperacidity, fever, ulcer, leprosy, and diuretic and also it has hepatoprotective activity [29]. This species of *Mussaenda* genus has wound healing property which has been proved in animal models (Excision, Incision and dead space models in rats) [30]. It also shows antibacterial activity against *Staphylococcus aureus* [26] *Escherichia coli*, *Pseudomonas aeruginosa* [31]. The dichloromethane extract of leaves shows antimicrobial activity against *Bacillus cereus*, *Bacillus subtilis*, *Saccharomyces cerevisiae* and the methanolic extract of leaves shows activity against *Bacillus cereus* and *Ustilago maydis*. The hexane extract of bark shows activity against *Bacillus cereus*, *Micrococcus luteus* and *Saccharomyces cerevisiae* [32].

The ethanolic extract of *M. frondosa* roots was found to possess normalizing activity against cold immobilization stress induced changes in norepinephrine, dopamine, 5-hydroxy tryptamine, 5-hydroxy indole acetic acid, and enzyme monoamine oxidase. It provides the biochemical evidence for antistress activity of the extract [33].

5.6. *Mussaenda roxburghii*

A new iridoid, shanzhiol, was isolated and identified from the aerial parts of *M. roxburghii* which shows mild antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* with a MIC of 100 µg/mL [34]. This species is useful for the treatment of infant sickness [35]. The root is used in the form of pill for the treatment of rheumatism [36]. Fresh leaf paste is applied topically to cuts and wounds, it also used in combination with other herbs to brew rice beer [37].

The chloroform soluble fraction has antimicrobial activity against *Bacillus megaterium* with maximum inhibition zone of 16.0 mm and MIC, MBC values of 7.81 µg/ml and 250 µg/ml, respectively. In the brine shrimp lethality

bioassay, the petroleum-ether and carbon tetrachloride soluble fraction of crude methanol extract shows cytotoxic activity with LC₅₀ value of 0.52 and 0.62 µg/ml respectively [38].

The antimicrobial, antioxidant and anti α -glucosidase activities of the leaf extract from *M. roxburghii* was evaluated. The result shows n-butanol and chloroform fractions has significant antioxidant activity against DPPH and superoxide radicals at the concentration of 100µg/ml and also exhibit maximum antimicrobial activity against *Vibrio cholerae* at 500 µg/disc. Both these fractions also exhibited moderate inhibition of α -glucosidase activity at the concentration of 500 µg/ml of n-butanol fraction and 250 µg/ml of chloroform fraction [39].

5.7. *Mussaenda macrophylla*

The phyto constituents of root bark include triterpenoid glycosides and their structures were determined as 3-O- β -D-glucopyranosyl-28-O-R-L-rhamnopyranosyl-16 α -hydroxy-23-deoxyprotobassic acid, 28-O- β -D-glucopyranosyl-16 α -hydroxy-23-deoxyprotobassic acid, 3-O- β -D-glucopyranosyl-28-O- α -L-rhamnopyranosyl-16 α -hydroxyprotobassic acid, and 3-O- $\{[\beta$ -D-glucopyranosyl-(1 \rightarrow 6)]-O- α -L-rhamnopyranosyl-(1 \rightarrow 2)-O- β -D-glucopyranosyl-(1 \rightarrow 2)}-O- β -D-glucopyranosyl-(1 \rightarrow 3)-O- β -Dglucopyranosyl-cycloarta-22,24-dien-27-oic acid, [3-O-acetyloleanolic acid, 3-O-acetyldaturadiol, rotundic acid, and 16 α -hydroxyprotobassic acid [40].

This plant has moderate inhibitory activity against the *Periodontopathic bacterium Porphyromonas gingivitis* with a MICvalue of 78µg/ml [41]. The carbon tetrachloride soluble fraction showed inhibition against *Salmonella paratyphi* and *Aspergillus niger* with the zone of inhibition of 15.0 and 13.0 respectively [42].

The methanol extract of the leaves of *M. macrophylla* and its petroleum ether, carbon tetrachloride, dichloromethane, ethyl acetate and aqueous soluble partitionates was evaluated for antioxidant activity by DPPH, Folin -Ciocalteu reagent and phosphomolybdenum total antioxidant assays by using butylated hydroxytoluene (BHT) and ascorbic acid as standards. It was found that dichloromethane soluble fraction has significant amount of phenolic compounds (38.50 \pm 0.64 mg GAE/g of extract) and also has moderate antioxidant activity (IC₅₀42.95 \pm 0.73 µg/ml) [43].

5.8. *Mussaenda dona-aurora*

The natural compound Sanshiside D was isolated from *M. dona-aurora*, which shows significant cytotoxicity on the growth of vero (African green monkey), HeLa and SMMC-7721 (human hepatoma) cell lines with IC₅₀value of 1.99, 0.12 and 1.53mM/ml respectively. This cytotoxicity of the iridoid was compared with commonly used drugs methotrexate and taxol having IC₅₀ of 3.89, 0.07, 1.37; 2.05, 0.05 and 0.74mM/ml, respectively [44].

5.9. *Mussaenda hainanensis*

The ethyl acetate, butanol and water extract of *M. hainanensis* has DPPH radical scavenging ability with the IC₅₀ (mg/ml) value of 0.0958, 0.4488, 0.9844. Twelve compounds from the extracts were identified and elucidated as pinostrobin, quercetin, 8-O-acetyl-shanzhiside methyl ester, 8[E]-N-[2'-hydroxyl-tetracosan- cosoyl]-1-O-- D-glucopyranosyl-8-en-octadecaspingene, caffeic acid, quercetin-3-O--D-glucosid, quercetin-7-O--D-glucoside, 3-O--D-gluco-pyranosyl pomolic acid 28-O--D-glucopyranosyl ester(8), 3,4-di-o-caffeoylquinic acid, chlorogenic acid, lamalbid, shanzhiside methyl ester [45]. The decoction of root can be administered orally to dispel the effects of alcohol [46].

5.10. *Mussaenda galbrata*

The phyto constituents reported from the leaves of *M. galbrata* includes saponin glucoside, resin, sugar, mucilage, coloring matter, quercetin, rutin, hyperin, β -sitosterol, glucoside, ferulic acid, sinapic acid. It is used for the treatment of jaundice and hepatitis [47]. Roots are given with cow's fresh milk for the treatment of leprosy. Whole plant is useful for diabetes patients. Flowers are used to treat swellings, conjunctivitis and asthma [48].

5.11. *Mussaenda queensirkit*

The cytotoxicity activity of methanolic extract of fresh flowers of *M.queensirkit* was evaluated. The result shows the maximum cytotoxicity at the concentration of 500 µg mL⁻¹ with 71.44% inhibition against fibroblast cultured from skin compared to the standard quercetin which exhibited a maximum of 92.7% inhibition. The HPLC profile reveals the presence of flavonol glycosides which may be responsible for the cytotoxic activity [49].

5.12. *Mussaenda parviflora*

The major constituents of leaf and root of *M. parviflora* were triterpenoids and it is useful for the treatment of malarial fever [50].

5.13. *Mussaenda flava*

The methanolic extract of *M. flava* flower shows more inhibition activity against *Bacillus subtilis* with the zone of inhibition of 20.0 mm [11].

5.14. *Mussaenda erosa* and *Mussaenda laxiflora*

These species were distributed in china, the decoction of stem, leaves and whole plant of *M. erosa* were used for the treatment of bruise, ulcer, burn, numbness of limbs and venereal disease. The decoction and alcoholic steeping of whole plant parts of *M. laxiflora* were used for the treatment of numbness of limbs, injuries from falls, rheumatoid arthritis, arthritis, hemiplegia, bellyache [7].

5.15. *Mussaenda hossei* and *Mussaenda multinervis*

These species were distributed in china, the raw decoction of root, leaf and bark of *M. hossei* were used for the treatment of Cough and burns. The decoction of root of *M. multinervis* can be administered orally with wine for the treatment of Backache and arthralgia [6].

5.16. *Mussaenda incana* and *Mussaenda esquirolli*

Two triterpene esters-3-palmitoyllupeol and 3-benzoylepibetulin along with β -sitosterol were isolated and identified from the stem of *M. incana* [51].

The GC-MS analysis of petroleum ether extracts of *M. esquirolli* has shown the presence of phytol (37.49%, 42.86%), squalene (5.59%, 47.15%), linolenic acid (9.79%) and β -sitosterol acetate (15.49%), as major chemical constituents which have high medicinal value [52].

CONCLUSION

The vast research done on the genus *Mussaenda* proved that many species has important phytoconstituents like flavonoids, glycosides, terpenoids, saponins etc. which has high therapeutic significance. The genus is widely used in traditional medicinal system and has been reported to possess hepatoprotective, anti-inflammatory, antimicrobial, antioxidant activity etc. It is important to consider that the genus *Mussaenda* is useful for treatment of wide spectrum of health problems in traditional and folk medicine; some of which have been experimentally validated. This review summarizes some important pharmacological studies on the genus *Mussaenda* and Phytoconstituents isolated from various species, which can be further investigated for the development of new novel herbal drugs.

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